

REMARKS/ARGUMENTS

Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments.

Claims 45, 47 and 48 have been amended to specify that the ubiquitous promoter is a polymerase III-dependent promoter in accordance with the specification at page 8, lines 4-13. Applicants do not believe that the amendments to these claims introduce any new matter. An early notice to that effect is earnestly solicited.

Claims 45 and 47 were rejected under 35 USC § 112, second paragraph, as being indefinite. In response, Applicants have amended claims 45 and 47 in a manner that Applicants believe clearly overcomes the Examiner's concerns. Thus, "construct" has been added after "said short hairpin RNA" in the last line of both claims. Also, the last line of claim 47 has been amended to refer to "said tissue or cell culture."

Claims 45, 47 and 48 were rejected under 35 USC § 102(e) as anticipated by or, in the alternative, under 35 USC § 103(a) as being obvious over Lowe et al. ("Lowe"), US 2008/0226553. In response, Applicants respectfully submit that Lowe does not anticipate or render obvious the subject matter of the rejected claims, as presently amended.

According to the Examiner, in the paragraph bridging pages 5-6 of the Office Action, "Lowe discloses an expression vector encoding a firefly luciferase shRNA construct flanked by two target sequences that target integration of the expression vector to the polymerase II-dependent, *hprt* gene locus of a mouse genome. Upon recombination integration of the

expression vector into the *hprt* gene locus the luciferase shRNA construct is operably linked to the ubiquitous mouse *hprt* promoter.”

Applicants believe it is clear, the Examiner’s interpretation being correct, that this means that in Lowe the shRNA construct is operably linked to the endogenous polymerase *hprt* promoter, a *polymerase II-dependent* promoter.

The rejected claims now require that the promoter is a heterologous *polymerase III-dependent* promoter and, thus, there is no anticipation.

Further, Applicants respectfully submit that given Lowe, it would not have been suggested to persons having ordinary skill in the art to combine a polymerase II-dependent locus with a heterologous polymerase III-dependent promoter with a reasonable expectation of success. A person having ordinary skill in the art would not have had a reasonable expectation that such a combination would provide for a successful and effective expression of a shRNA construct. Moreover, as can be seen from the experimental portion of the instant application, the polymerase II locus in combination with a heterologous polymerase III-dependent locus provides for efficient repression of a target gene through expression of the appropriate shRNA construct (see Example 4).

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has been reconsidered and withdrawn is earnestly solicited.

Applicants believe that the foregoing constitutes a bona fide response to all outstanding objections and rejections.

Applicants also believe that this application is in condition for immediate allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,
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